TP53 gene

tumor protein p53

Normal Function

The *TP53* gene provides instructions for making a protein called tumor protein p53 (or p53). This protein acts as a tumor suppressor, which means that it regulates cell division by keeping cells from growing and dividing too fast or in an uncontrolled way.

The p53 protein is located in the nucleus of cells throughout the body, where it attaches (binds) directly to DNA. When the DNA in a cell becomes damaged by agents such as toxic chemicals, radiation, or ultraviolet (UV) rays from sunlight, this protein plays a critical role in determining whether the DNA will be repaired or the damaged cell will self-destruct (undergo apoptosis). If the DNA can be repaired, p53 activates other genes to fix the damage. If the DNA cannot be repaired, this protein prevents the cell from dividing and signals it to undergo apoptosis. By stopping cells with mutated or damaged DNA from dividing, p53 helps prevent the development of tumors.

Because p53 is essential for regulating cell division and preventing tumor formation, it has been nicknamed the "guardian of the genome."

Health Conditions Related to Genetic Changes

bladder cancer

Somatic *TP53* gene mutations have been found in some cases of bladder cancer. Most of these mutations change single amino acids in p53. The altered protein cannot bind to DNA, preventing it from effectively regulating cell growth and division. As a result, DNA damage accumulates in cells, which can allow them to grow and divide in an uncontrolled way to form a cancerous tumor. Mutations in the *TP53* gene may help predict whether bladder cancer will progress and spread to nearby tissues, and whether the disease will recur after treatment.

breast cancer

Inherited changes in the *TP53* gene greatly increase the risk of developing breast cancer, as well as several other forms of cancer, as part of a rare cancer syndrome called Li-Fraumeni syndrome (described below). These mutations are thought to account for only a small fraction of all breast cancer cases.

Noninherited (somatic) mutations in the *TP53* gene are much more common than inherited mutations, occurring in 20 to 40 percent of all breast cancers. These somatic mutations are acquired during a person's lifetime and are present only in

cells that become cancerous. The cancers associated with somatic mutations do not occur as part of a cancer syndrome. Most of these mutations change single protein building blocks (amino acids) in the p53 protein, which reduces or eliminates the protein's tumor suppressor function. Because the altered protein is less able to regulate cell growth and division, DNA damage can accumulate. This damage may contribute to the development of a cancerous tumor by allowing cells to grow and divide in an uncontrolled way.

Compared with breast cancers without *TP53* gene mutations, tumors with these genetic changes tend to have a poorer prognosis. They are more likely to be aggressive, to be resistant to treatment with certain anti-cancer drugs and radiation, and to come back (recur) after treatment.

cholangiocarcinoma

head and neck squamous cell carcinoma

Somatic mutations in the *TP53* gene have been found in nearly half of all head and neck squamous cell carcinomas (HNSCC). This type of cancerous tumor occurs in the moist lining of the mouth, nose, and throat. Most of the *TP53* gene mutations involved in HNSCC change single amino acids in p53; these changes impair the protein's function. Without functioning p53, DNA damage builds up in cells, and they can continue to divide without control, leading to tumor formation.

Li-Fraumeni syndrome

Although somatic mutations in the *TP53* gene are found in many types of cancer, Li-Fraumeni syndrome appears to be the only cancer syndrome associated with inherited mutations in this gene. This condition greatly increases the risk of developing several types of cancer, particularly in children and young adults. At least 140 different mutations in the *TP53* gene have been identified in individuals with Li-Fraumeni syndrome.

Many of the mutations associated with Li-Fraumeni syndrome change single amino acids in the part of the p53 protein that binds to DNA. Other mutations delete small amounts of DNA from the gene. Mutations in the *TP53* gene lead to a version of p53 that cannot regulate cell growth and division effectively. Specifically, the altered protein is unable to trigger apoptosis in cells with mutated or damaged DNA. As a result, DNA damage can accumulate in cells. Such cells may continue to divide in an uncontrolled way, leading to the growth of tumors.

ovarian cancer

Somatic *TP53* gene mutations are common in ovarian cancer, occurring in almost half of ovarian tumors. These mutations result in a p53 protein that is less able to control cell growth and division, contributing to the development of a cancerous tumor.

other cancers

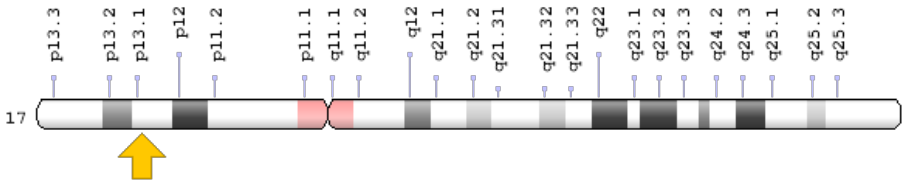
Somatic mutations in the *TP53* gene are the most common genetic changes found in human cancer, occurring in about half of all cancers. In addition to the cancers described above, somatic *TP53* gene mutations have been identified in several types of brain tumor, colorectal cancer, liver cancer, lung cancer, a type of bone cancer called osteosarcoma, a cancer of muscle tissue called rhabdomyocarcinoma, and a cancer called adrenocortical carcinoma that affects the outer layer of the adrenal glands (small hormone-producing glands on top of each kidney).

Most *TP53* mutations change single amino acids in the p53 protein, which leads to the production of an altered version of the protein that cannot control cell growth and division effectively. As a result, cells can grow and divide in an unregulated way, which can lead to cancerous tumors.

Chromosomal Location

Cytogenetic Location: 17p13.1, which is the short (p) arm of chromosome 17 at position 13.1

Molecular Location: base pairs 7,668,402 to 7,687,550 on chromosome 17 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- antigen NY-CO-13
- cellular tumor antigen p53
- P53
- P53 tumor suppressor
- P53_HUMAN
- phosphoprotein p53
- transformation-related protein 53
- TRP53

- tumor protein p53 (Li-Fraumeni syndrome)
- tumor suppressor p53

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): Cell-Cycle Progression is Blocked by DNA Damage and p53: DNA Damage Checkpoints
  https://www.ncbi.nlm.nih.gov/books/NBK26856/#A3240
- Molecular Cell Biology (fourth edition, 2000): Mutations in p53 Abolish G1 Checkpoint Control
  https://www.ncbi.nlm.nih.gov/books/NBK21551/#A7158
- National Cancer Institute: Genetics of Breast and Gynecologic Cancers (PDQ)
  https://www.cancer.gov/types/breast/hp/breast-ovarian-genetics-pdq

GeneReviews

- Li-Fraumeni Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1311

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28TP53%5BTI%5D%29+OR+%28p53%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+180+days%22%5Bdp%5D

OMIM

- TUMOR PROTEIN p53
  http://omim.org/entry/191170

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/P53ID88.html
- Cancer Genetics Web: TP53
  http://www.cancerindex.org/geneweb/TP53.htm
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=TP53%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=11998

- IARC TP53 Mutation Database
  http://p53.iarc.fr/
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/7157
- p53 Web Site (Thierry Soussi)
  http://p53.fr/
- UniProt
  http://www.uniprot.org/uniprot/P04637

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